



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 15/52, 5/10, 9/64, C12Q 1/37, 1/68, A61K 31/70, 38/43, A01K 67/027, G01N 33/50	A3	(11) International Publication Number: WO 00/04157 (43) International Publication Date: 27 January 2000 (27.01.00)
(21) International Application Number: PCT/GB99/02241 (22) International Filing Date: 14 July 1999 (14.07.99) (30) Priority Data: 9815284.6 14 July 1998 (14.07.98) GB (71) Applicant (for all designated States except US): JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE). (72) Inventors; and (75) Inventors/Applicants (for US only): PANGALOS, Menlas [GB/GB]; 136 Beaufort Park, London NW11 6DA (GB). NEEFS, Jean-Marc, Edmond, Fernand, Marie [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). PEETERS, Danielle, Celine, Georgette [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). (74) Agent: BOULT WADE TENNANT; 27 Fumival Street, London EC4A 1PQ (GB).	(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 27 July 2000 (27.07.00)	
(54) Title: CLONING AND CHARACTERISATION OF NOVEL MAMMALIAN PEPTIDASES (57) Abstract <p>There is disclosed a cDNA molecule encoding human NAALAD-ases designated herein as L, II and IV and having the amino acid sequences illustrated in Figures 1, 3, 4 and 5. The NAALAD-ases themselves also form part of the invention. Further provided are expression vectors incorporating the cDNA molecules suitable for transforming a cell, tissue or organism.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/02241

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/52 C12N5/10 C12N9/64 C12Q1/37 C12Q1/68
A61K31/70 A61K38/43 A01K67/027 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SHNEIDER B.L. ET AL.: "Cloning and characterization of a novel peptidase from rat and human ileum." J. BIOL. CHEM., vol. 272, no. 49, 5 December 1997 (1997-12-05), pages 31006-31015, XP002129302 cited in the application the whole document	1-4, 9-11, 18-29, 34-36, 41-44
A	LUTHI-CARTER R. ET AL.: "Isolation and characterization of a rat brain cDNA encoding glutamate carboxypeptidase II" PROC. NATL. ACAD. SCI. USA, vol. 95, March 1998 (1998-03), pages 3215-3220, XP002129303 cited in the application the whole document	1-4, 9-11, 18-29, 34-36, 41-44

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

31 January 2000

Date of mailing of the international search report

11. 05. 2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Galli, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/02241

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CARTER R.E. ET AL.: "Prostate-specific membrane antigen is a hydrolase with substrate and pharmacologic characteristics of a neuropeptidase." PROC. NATL. ACAD. SCI. USA, vol. 93, January 1996 (1996-01), pages 749-753, XP002129304 cited in the application the whole document	1-4, 9-11, 18-29, 34-36, 41-44
A	WO 96 15258 A (UPJOHN CO ;ELHAMMER AKE P (US)) 23 May 1996 (1996-05-23) abstract	41-44
P,X	PANGALOS M.N. ETAL.: "Isolation and expression of novel human glutamate carboxypeptidases with N-acetylated alpha-linked acidic dipeptidase and dipeptidyl peptidase IV activity." J. BIOL. CHEM., vol. 274, no. 13, 26 March 1999 (1999-03-26), pages 8470-8483, XP002129305 the whole document	1-4, 9-11, 18-29, 34-36, 41-44

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/02241

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-4, 10, 11 (complete); 9, 18-48 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: (1-4,10,11) - completely; (9,18-48) - partially

A cDNA molecule encoding a human NAALADase-L protein or a functional equivalent, derivative or bioprecursor thereof.

Corresponding coding sequences, vectors, recombinant host cells, therapeutic and pharmaceutical applications thereof, use in methods to identify agonists and antagonists, agonists and antagonists, use in enzymologic methods.

2. Claims: (5,6,12-14) - completely; (9,18-48) - partially

Idem as subject-matter 1 but limited to NAALADase II

3. Claims: (7,8,15-17) - completely; (9,18-48) - partially

Idem as subject-matter 1 but limited to NAALADase IV

4. Claims: (41,43) - partially

As far as not covered by inventions 1-3:

A method for quantifying enzyme activity which comprises contacting an enzyme of interest with a radiolabelled hydrolysable substrate thereof in the presence of scintillation proximity assay beads (SPA).

Said method, wherein said substrate is 3H-NAAG and said enzyme comprises a NAALADase.

5. Claims: (42,43) - partially

As far as not covered by inventions 1-3:

A method of identifying a compound which is an inhibitor or an enhancer of activity of an enzyme, comprising contacting an enzyme of interest with a radiolabelled hydrolysable substrate thereof and said compound to be tested in the presence of scintillation proximity assay beads (SPA), stopping the reaction by adding glycine buffer, and monitoring the signal from the substrate bound to said beads compared to a control.

Said method, wherein said substrate is 3H-NAAG and said enzyme comprises a NAALADase.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 3.

Claims Nos.: 30-33,37-40,45-48

Claims 30-33, 37-40 and 45-48 refer to agonists and antagonists of the NAALADases claimed without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/02241

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9615258 A	23-05-1996	US 5861318 A	19-01-1999
		AT 191012 T	15-04-2000
		AU 4278196 A	06-06-1996
		DE 69515901 D	27-04-2000
		EP 0792373 A	03-09-1997
		JP 10508749 T	02-09-1998
